

U.S.S.N. 08/249,689
Filed May 26, 1994
AMENDMENT

In the Claims

1. (previously presented) A method for designing a compound specifically inhibiting targeted ribonucleic acid function comprising the steps of:
- (a) determining the nucleotide sequence in the targeted ribonucleic acid that is critical to function;
 - (b) determining the secondary structure of the region of the targeted ribonucleic acid in which the critical site is located;
 - (c) determining the three-dimensional structure of the targeted RNA, including the position of the critical site relative to the major and minor grooves;
 - (d) determining the sequence of nucleotides and structure flanking the critical site in the targeted ribonucleic acid that is specific to the critical region of the ribonucleic acid to be inhibited and within the minor groove; and
 - (e) synthesizing a compound that will bind specifically to the critical site within the minor groove of the targeted ribonucleic acid thereby inhibiting targeted ribonucleic acid function.
2. (canceled)
3. (original) The method of claim 1 wherein the ribonucleic acid is selected from the group consisting of mRNA, rRNA, tRNA and viral RNA.
4. (previously presented) The method of claim 1 wherein inhibition of targeted ribonucleic acid function inhibits protein synthesis.

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5. (previously presented) The method of claim 4 wherein protein synthesis is inhibited in cells selected from the group consisting of tumor cells, virally infected cells, and bacterial cells.

6. (original) The method of claim 1 wherein the three-dimensional structure is modeled using sequences of the RNA and calculating the minimum energies for these structures.

7. (previously presented) The method of claim 1 wherein the critical region of the targeted ribonucleic acid is determined by mutation of regions of the targeted RNA and comparison of the function of the mutated RNA with the original RNA, wherein mutations that result in mutant RNA having altered function indicate that the site of mutation is a critical site.

8. (original) The method of claim 1 wherein the targeted RNA is a tRNA, wherein the critical region of the tRNA is determined by site directed mutation of the tRNA and analysis of the function of the mutated tRNA.

9. (previously presented) The method of claim 1 further comprising determining an effective amount of the compound and combining the compound with a pharmaceutical carrier.

10. (previously presented) The method of claim 9 wherein the carrier is selected from the group consisting of pharmaceutically acceptable compositions for topical administration, pharmaceutically acceptable compositions for parenteral administration, pharmaceutically acceptable compositions for enteral administration, and combinations thereof.

11. (currently amended) A complementary compound comprising hydrogen bond donor and acceptor sites arranged to specifically bind and inhibit the function of a targeted RNA molecule, wherein the compound is specifically directed to and binds to a critical region within

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~~the minor groove of the acceptor stem of a tRNA molecule of the RNA molecule, located within~~
~~the minor groove of the RNA molecule,~~ identified by a combination of the primary, secondary
and tertiary structure of the critical region.

12. (canceled)

13. (previously presented) The complementary compound of claim 11 further
comprising a pharmaceutically acceptable carrier selected from the group consisting of
pharmaceutically acceptable compositions for topical administration, pharmaceutically
acceptable compositions for parenteral administration, pharmaceutically acceptable compositions
for enteral administration, and combinations thereof.

14. (previously presented) The method of claim 3 wherein the critical site is in the
minor groove of the acceptor stem of a tRNA molecule.

15. (previously presented) The method of claim 14 wherein the tRNA molecule is
tRNA^{Ala}.

16. (previously presented) The method of claim 15 wherein the critical site is the
G3:U70 base pair.

17. (canceled)

18. (currently amended) The complementary compound of claim ~~17~~ 11 wherein the
tRNA molecule is tRNA^{Ala}.

19. (currently amended) The complementary compound of claim ~~17~~ 11 wherein the
critical region is the G3:U70 base pair.

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20. (previously presented) The method of claim 1 wherein the compound is a nucleic acid and the compound is synthesized *in vivo* from a retroviral vector.

21. (previously presented) The complementary compound of claim 11 wherein the compound is a nucleic acid and the compound is synthesized *in vivo* from a retroviral vector.

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